REMARKS

Claims 1-6, 8-11 and 18 are pending and under active consideration in the instant application. Claims 1, 8, 9, and 18 have been amended to clarify the subject matter of the present claims. Support for the amendments to claims 1, 8, 9, and 18 can be found in the specification, *inter alia*, at paragraphs [0028], [0125], and [0192].

Applicants request that the amendments and remarks made herein be entered and made of record in the file of the above-identified application.

THE REJECTION UNDER 35 U.S.C. § 102(a) SHOULD BE WITHDRAWN

The Examiner has rejected claims 1-11[1] and 18 under 35 U.S.C. § 102(a) as anticipated by Okamoto *et al.*, 2002, Science 5:643-649 ("Okamoto") in light of Veech, U.S. Patent No. 4,663,289 ("Veech") and Male *et al.*, U.S. Patent No. 5,292,524 ("Male"). Applicants submit that the rejection under Okamoto is in error for the reasons set forth below.

For reasons of record, Applicants maintain that Okamoto fails to anticipate the invention as claimed. Nevertheless, without agreeing with the Examiner and merely to advance prosecution, Applicants have amended the claims to clarify that the poly-β-1→4-N-acetylglucosamine ("p-GlcNAc") polymer and/or fiber encompassed by the present invention is distinct from the chitin or chitosan of the prior art. In particular, Applicants have amended the pending independent claim 1 to recite, in part, that the claimed composition comprises a **biocompatible** p-GlcNAc polymer; claims 8 and 9 to recite, in part, that the composition comprises a **biocompatible** p-GlcNAc fiber; and claim 18 to recite, in part, the method comprises mixing a **biocompatible** fiber slurry. Applicants submit that, as used in the instant specification, purified p-GlcNAc would be understood by one of skill in the art to be biocompatible. Thus, the amendments to claims 1, 8, 9, and 18 do not limit the scope of these claims.

Despite the Examiner's contention that Applicants have asserted that chitin consists in part of p-GlcNAc (see Office Action, page 3, lines 12-13). Applicants respectfully submit that the instant specification specifically distinguishes the chitin of the prior art from the purified biocompatible p-GlcNAc as recited in the instant claims. Although chitins, chitosans, and p-GlcNAc are all polymers of monosaccharide sugars attached in a β-1→4

[1] Applicants note that claim 7 was cancelled in the Amendment under 37 C.F.R. § 1.111 filed February 13, 2006.

conformation, unlike p-GlcNAc, materials derived from chitin and chitosan differ widely in terms of physical and chemical properties; exhibit varying molecular weights and degrees of acetylation; and contain contaminants such as *covalently* bound, species specific proteins, single amino-acids and inorganic contaminants (see specification , at paragraph [003]). Such variability and contamination have rendered chitin and chitosan based products especially unsuitable for medical uses (*see* specification, [004] to [006]). Moreover, prior art compositions derived from chitin and chitosans had not been approved as of the effective filing date of the present application for such purposes due to the difficulties in obtaining consistent preparations suitable for *in-vivo* use (discussed, *e.g.*, in Chapter 4 of "Barriers to Commercialization" in Chitin and Chitosan (Technical Insights, Inc., Engewood/ Fort Lee N.J.), a copy of which is enclosed herewith as Exhibit B). In contrast, the biocompatible p-GlcNAc as instantly claimed has been approved by the U.S. Food and Drug Administration ("FDA") for a variety of biomedical uses. Thus, Okamoto's teaching of chitin is not a teaching of a biocompatible poly-β-1→4-N-acetylglucosamine as instantly claimed. Accordingly, Okamoto does not anticipate any of claims 1-6, 8-11, and 18.

The Examiner cites U.S. Patent No. 4,663,289 to Veech ("Veech") and U.S. Patent No. 5,292,524 to Male ("Male") in support of her position that Okamoto anticipates the present claims. Veech relates to cell culture/preservation media and Male relates to the use of platelets as therapeutic agents. As noted by the Examiner, Veech and Male respectively describe the calcium content of blood plasma and modified Tyrode's Buffer used in Okamoto. However, for the foregoing reasons, Okamoto does not anticipate the invention as claimed herein because Okamoto does not teach a biocompatible p-GlcNAc polymer, fiber or fiber slurry, which lack of teaching neither Veech nor Male supplement.

For at least the foregoing reasons, Okamoto does not teach each and every element of independent claims 1, 8, 9, and 18, as amended herein. Accordingly, Okamoto cannot anticipate the claims. Because Okamoto does not anticipate any of independent claims 1, 8, 9, and 18, the reference also does not any claim dependent from these claims.

Applicants therefore respectfully submit that the rejection of claims 1-6, 8-11 and 18 as anticipated by Okamoto in light of Veech and Male is in error and should be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

All pending claims are rejected under 35 U.S.C. § 103 as obvious over two different combinations of references, which are discussed below.

To establish a *prima facie* case of obviousness, the teachings of the prior art must provide one of ordinary skill in the art with some suggestion or motivation to make the claimed composition. *In re Rijckaert*, 28 U.S.P.Q.2d 1955, 1956 (Fed. Cir. 1993). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). When a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references. *In re Rouffet*, 149 F.3d 1350 (Fed. Cir. 1998). Further, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974).

"Measuring a claimed invention against the standard established by section 103 requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field." *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir.1999), abrogated on other grounds, citing to *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553 (Fed. Cir. 1983). In particular, the Examiner cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988). Care must be taken to avoid hindsight reconstruction by using Applicants' disclosure "as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result" of the claims in question. *Grain Processing Corporation v. American Maize-Products Company*, 840 F.2d 902, 907 (Fed.Cir.1988), citing *Orthopedic Equip. Co. v. United States*, 702 F.2d 1005, 1012 (Fed.Cir.1983).

Applicants submit that, the Examiner, in raising the obviousness rejections, is employing, perhaps unconsciously, a hindsight reconstruction without casting her mind to the state of the art at the time of filing the present application. As stated above, such hindsight reconstruction does not meet the legal standard for obviousness. Each of the combinations cited by the Examiner is discussed in turn below to demonstrate that, standing in the shoes of

the Applicants at the time the present application was filed, there was no suggestion of or motivation in the art to practice the claimed invention.

The Rejection over Cochrum and Vournakis in view of Veech and Male

The Examiner has rejected claims 1-11[1], 15, 17 and 18 under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,614,204 to Cochrum ("Cochrum") in combination with U.S. Patent No. 5,858,350 to Vournakis *et al.*, ("Vournakis") in light of Veech and Male. Applicants respectfully disagree with the Examiner's rejection for the reasons outlined below.

In Cochrum, biopolymers, including chitosan, are used alone or combined with platelet rich plasma ("PRP") and administered intravenously in the proximity of bleeding, a rupture, a fistula, etc. to form an occlusive clot. However, as recognized by the Examiner (*see*, Office Action at page 7, lines 9-10), nowhere in Cochrum is any suggestion or motivation for making a composition comprised of biocompatible p-GlcNAc and platelets as required by the claims as amended herein. Accordingly, Cochrum does not render obvious the invention of amended independent claims 1, 8, 9, and 18. Because the reference does not render obvious the invention as claimed in amended independent claims 1, 8, 9, and 18, Cochrum does also not render obvious any of the pending claims dependent thereon, *i.e.*, claims 2-6 and 10-11.

Vournakis does not remedy the deficiencies of Cochrum. Vournakis is directed to various uses of p-GlcNAc, including its use as a hemostatic device. However, while Vournakis teaches the application of a p-GlcNAc to a patient to stop bleeding, the reference provides no suggestion or motivation to form a composition comprising p-GlcNAc and platelets as recited in claims 1-6, 8-11, or a method for producing a gel comprised of p-GlcNAc and platelets, as recited in claim 18. Accordingly, Vournakis, whether alone or in combination with Cochrum fails to render obvious the invention as claimed in claims 1-6, 8-11, and 18.

Neither Veech nor Male remedy the deficiencies of Cochrum alone or in combination with Vournakis. As previously discussed, Veech relates to cell culture/preservation media and Male relates to the use of platelets as therapeutic agents. Neither teaches nor relates to the use or manufacture of a composition of poly-β-1→4-N-acetylglucosamine with platelets. Since none of the references cited by the Examiner, alone or in combination, teach a composition comprising biocompatible p-GlcNAc and platelets, the rejection is in error.

Applicants therefore respectfully submit that the rejection of claims 1-6, 8-11, 15, 17 and 18 over Cochrum in combination with Vournakis in view of Veech and Male is in error and should be withdrawn.

The Rejection over Okamoto and Vournakis in view of Veech and Male

The Examiner has also rejected claims 1-11[1], and 18 under 35 U.S.C. § 103(a) as obvious over Okamoto in combination with Vournakis in light of Veech and Male. Applicants disagree with the Examiner's rejection for the following reasons.

Okamoto provides a study of the effect of chitin or chitosan particle on platelet compositions (*see* Okamoto Abstract and Experimental section, page 643, lines 2-3). In particular, contact of platelets with the chitin or chitosan suspensions was found to induce both aggregation and activation of platelets. Notably, the chitin-platelet composition is the end result of Okamoto's study, and nowhere does Okamoto provide a teaching or suggestion for the use of such a composition. At most, Okamoto suggests that chitin or chitosan is itself useful as a coagulation or activation agent. Thus, Okamoto does not provide any suggestion or motivation for making a composition comprising chitin or chitosan and platelets, much less the motivation for combining biocompatible p-GlcNAc polymer and platelets for therapeutic or platelet preservation applications. Accordingly Okamoto does not render obvious the invention of claims 1-6, 8-11 and 18.

The Examiner further references Cochrum wherein compositions of chitin and PRP are used to form vascular occlusions. For reasons previously discussed, Applicants submit that Cochrum fails to render obvious the claimed invention. In particular, Cochrum provides no suggestion for the use of a biocompatible p-GlcNAc. Therefore, Cochrum, whether alone or in combination with Okamoto, fails to render obvious the presently claimed invention.

Vournakis fails to remedy the deficiencies of Okamoto, alone or in combination with Cochrum. As discussed *supra*, Vournakis neither teaches or suggests the use of a composition comprising p-GlcNAc and platelets. Accordingly, the rejection over Okamoto and Cochrum, alone or in combination with Vournakis is in error.

Neither Veech nor Male remedy the deficiencies of Okamoto, Cochrum and Vournakis, alone or in combination, for reasons previously discussed. In particular, Veech relates to cell culture/preservation media and Male relates to the use of platelets as

therapeutic agents. Neither reference teaches or relates to the use or manufacture of a composition of poly-β-1→4-N-acetylglucosamine with platelets.

For the foregoing reasons, Applicants submit that the rejection of claims 1-6, 8-11 and 18 over Okamoto in combination with Cochrum, in further combination with Vournakis and in view of Veech and Male is in error and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted, by: RICHARD ENMON, Jr. 52,865

Date: October 17, 2006

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4 BARRIERS TO COMMERCIALIZATION

Significant barriers to commercialization have slowed the introduction of chitin and chitosan products. Some of these are being overcome; others will continue to hinder commercialization. Below we discuss the most significant barriers to be overcome and possible ways these barriers might be overcome.

4.1 SUPPLY LIMITATIONS

Some people in the industry call this the "chicken and the egg" problem: Which do you develop first, the supply of chitin and chitosan or the end uses? Right now there is an oversupply of chitin/chitosan on world markets. However, some companies hesitate to use chitin or chitosan in their products due to concern that widespread commercialization will lead to shortages. Even if commercial plants are built to process shellfish wastes to chitin and chitosan, there is only a limited supply of shellfish wastes that could be used as raw material. The estimated global supply of accessible chitin is 150,000 metric tons. The seasonality of the shellfish supply could precipitate shortages, unless producers develop supply agreements with shellfish processors in different locations and collect these efficiently for centralized processing.

A few researchers are trying to develop alternative sources of the material. Fungal fermentation is a major potential source, but is currently more expensive than deriving the material from shellfish waste. Genetic engineering may enhance productivity of fungal strains or make the product easier to extract. But it may not

result in strains from which chitin or chitosan can be produced as cheaply as from shellfish waste.

4.2 COSTS

Chitin and chitosan are expensive compared to other polymers, and production costs are likely to remain near current levels. As a result, companies will have to develop products that are appropriately priced for particular applications. For example, material marketed for agricultural applications will be of lower quality, and thus lower price, than material destined for a high-value medical application.

4.3 NEED FOR HIGH-VALUE MARKET NICHES

Lower priced products may be developed for a few applications, but most will require a higher-value niche in which chitin or chitosan has a clear advantage over competing products. As a result, companies need to develop end uses that will support higher costs. That is one reason that high-value medical applications are a primary area of investigation. For uses such as water treatment, which generally does not command higher priced materials, chitosan products will penetrate primarily higher-value niches. The performance of synthetic polymers is adequate for most water treatment uses, so a premium product like chitosan isn't likely to gain widespread use. Regulatory changes and changes in the use of related technologies could however, create new niches. For example, in Japan, the use of chitosan in water treatment is more

widespread due to regulation of synthetic alternatives and greate use of incineration as a disposal method, Other market niches ma develop where chitin or chitosan has a clear advantage -- where there is no less expensive product that will perform adequately.

4.4 VARIABILITY IN QUALITY

Chitin and chitosan are made by a variety of producers from many different shellfish sources. Thus the properties of the finished products may vary, either due to the particular productio process used or due to the source. Chitin naturally comes in two different basic orientations and each sample has varying levels of microcrystalline segments in the polymer chain. Chitin and chitosan both vary in their levels of acetylation.

Companies using the material in particular applications need tc know that the quality will be consistent. This is particularly important in high value uses such as medical applications, where poor quality material could have adverse effects. Inconsistent quality is also an obstacle to regulatory approval. If authorities approve a product based on clinical data, they need to know that the commercial product will be identical to that used in the clinical studies.

Some people see fungal fermentation processes as a possible solution to this problem. A genetically engineered strain might be modified to produce more chitin or chitosan and fewer other products. Current fermentation strains may contain just as many impurities as shellfish-derived chitosan, but the identity of the impurities is probably different.

4.5 LACK OF METHODS TO CHARACTERIZE

Even if consistent quality of material is available, methods are needed to characterize the material, demonstrating that consistency. If such methods were available, products could be evaluated objectively and standards established for particular applications.

4.6 NEED FOR REGULATORY APROVAL

Getting approval of the U.S. Food and Drug Administration for chitosan products will probably cost millions of dollars. Most companies either do not have enough capital or are unwilling to make that large an investment. Food applications will be held back most, because profits on food products are generally smaller than those on medical products. Also, companies will want to avoid investing large sums into gaining approval, only to see their competitors introduce competing products for the approved end uses. One possibility that could help is the establishment of GRAS (generally recognized as safe) status for chitin. However, the derivative chitosan, which is used in most commercial applications won't qualify for GRAS status.

Outside the United States, regulatory approval is often less costly. In addition, companies may find it easier to bypass regulatory approval. For example, Japanese attitudes toward natural products allow companies to use chitin in food uses without conducting extensive human trials. The ingredient is generally labeled in a way that emphasizes its natural character -- for exam-

ple, as shellfish derivative. In Japan natural products are generally perceived as safe.

4.7 POLLUTION PROBLEMS

Companies often see chitin products as a solution to the problem of disposal of shellfish waste. The process does reduce the volume of the material. But after you extract chitin from shellfish, you still have shells full of lye or acid (depending on the extraction process). Companies producing chitin and chitosan will have to face up to this new waste problem by finding effective methods for disposing of mineral and protein wastes left from the process. In addition, fungal fermentations might result in easier-to-process waste.

4.8 TRADE BARRIERS

Worldwide marketing of chitin and chitosan products is in some cases hampered by trade barriers. For example, Soviet companies desiring to market the products in the United States are subject to a 50% import duty. This problem is significant because some chitin and chitosan producers are located in countries in which demand for the end product is fairly low. Other countries may develop a strong demand for the products but have an undersupply of raw materials.

Companies will probably solve this problem by developing international relationships with companies in other countries. For example, a Soviet company could import chitin to Canada, process it

into chitosan there, and then import it into the United States as Canadian product.

4.9 DIFFICULTY GETTING PATENTS

Because chitin is the second most abundant natural polymer a because it has been studied for decades, a tremendous number of articles and patents exist in the field. This makes it difficul to get new patents, especially on chitin production processes. Even if you have unique aspects to your process, it is difficult prove that they are unique.

4.10 NEED TO DEVELOP ASSOCIATED TECHNOLOGY

In some cases, users of chitin or chitosan need support technology developed specifically for use with chitin or chitosan. example, treatment of seeds with chitosan requires special equipment. If the proper equipment is not used, the seed coating is uniform and may not give the right dosage. The likely result: inconsistent effects of the chitosan product.

4.11 POLITICAL CLIMATE

The present political climate in the United States, and many other countries, does not demand products that are, biodegradabl nontoxic, and natural. In some end uses, such as food, this may changing. A greater support for naturally produced materials co push chitin products toward market.